Polymorphic Ventricular Tachycardia with Cardiac Sarcoidosis: Treatment with Low-Dose Metoprolol and Cibenzoline

Mitsunori Okamoto, Masaki Hashimoto, Takashi Sueda, Makoto Munemori and Tadakatsu Yamada

A 38-year-old female had felt exertional dyspnea for six months. Physical examination and laboratory data, including angiotensin-converting enzyme, failed to diagnose sarcoidosis. Her chest X-ray showed cardiomegaly but no hilar lymph node enlargement. Holter ECG showed nonsustained and sustained ventricular tachycardias, monomorphic or polymorphic tachycardia. Echocardiography and contrast left ventriculography showed left ventricular dilatation and generalized hypo- and akinesis. Endomyocardial biopsy revealed myocardial sarcoidosis. Administration of corticosteroids, metoprolol of 20 mg/day and cibenzoline of 300 mg/day was markedly effective for the treatment of ventricular tachycardia. This patient is alive for one year after treatment and the combination therapy seems to contribute to good prognosis.

Key words: torsades de pointes, B-blockers

Introduction

Cardiac sarcoidosis was first described by Bernstein in 1929 (1). It constituted 20% of sarcoid patients (2). Electrocardiographic findings in cardiac sarcoidosis included ventricular premature beats, ventricular tachycardia and fibrillation, AV block, conduction defects and ST-T changes (3–5). However, in previous reports we could not find polymorphic ventricular tachycardias in cardiac sarcoidosis. We treated a patient with cardiac sarcoidosis who had frequent ventricular tachy-arrhythmias of monomorphic or polymorphic form, where combination therapy of low-dose metoprolol, cibenzoline and corticosteroids was effective for the treatment of tachy-arrhythmias.

Case Report

A 38-year-old female had complained of palpitation and exertional dyspnea for about six months. Physical examination revealed an irregular radial pulse of about 70/min. Her blood pressure as measured by a sphygmomanometer was 102/60 mmHg in the right brachial artery. Uveitis was not found by an ophthalmologist. Skin rash was not observed. The jugular veins were slightly engorged, but enlarged lymph nodes were not palpable anywhere. Cardiac dullness was extended and third heart sound was audible. No peripheral edema was evident.

Hepatomegaly and splenomegaly were not found. Electrocardiography showed premature ventricular beats, left atrial overloading, Q wave in leads I and aVL, and negative T in leads I, II, III, aV1, AVF and V4–V5. PQ interval was 0.20 seconds, QRS 0.10 seconds and QTc 0.44 seconds (Fig. 1). Chest X-ray showed cardiomegaly and slight pulmonary venous congestion but there was no hilar lymph node enlargement. Cardiothoracic ratio was 60%. In Holter ECG, 6,462 premature ventricular beats, 1,154 couplets of premature ventricular beats and 678 nonsustained ventricular tachycardias a day were observed (Table 1). Some ventricular tachycardias were polymorphic (Fig. 2). Echocardiography demonstrated a dilated and generally hypo- or akinetic left ventricle. The left ventricular diastolic dimension was 67 mm with an interventricular septal thickness of 4.3 mm and posterior wall thickness of 6.9 mm. Ejection fraction was 19%. 201Tl scintigraphy showed multiple defects of uptake. Coronary angiography revealed no stenosis of the coronary arteries and left ventriculography showed generalized hypo- and akinesis of the left ventricle. Endomyocardial biopsy specimen from the right ventricle disclosed the existence of myocardial involvement of sarcoidosis (Fig. 3). Scalen node biopsy specimen also indicated the infiltration of sarcoidosis.

In laboratory examination findings, CRP and erythrocyte sedimentation rate were normal. Serum sodium was 140 mEq/l, serum potassium 3.7 mEq/l, serum calcium 4.7 mEq/l, serum chloride 105 mEq/l, serum urea nitrogen 11.3 mg/dl and
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Creatinine 0.7 mg/dl. CPK was 26 (24–195) μl and LDH 272 mU/ml. Myosin light chain was 1.0 (<2.5) ng/ml. IgG was 1,527 mg/dl, IgA 194 mg/dl and IgM 213 mg/dl. Angiotensin-converting enzyme was 15.6 (<20) U/ml and OKT4/OKT8 ratio was 1.72 (1.18–2.00). The above laboratory data were all normal. Tuberculin skin test was 7x8 mm.

Clinical course

The patient was admitted on February 9, 1992 with sustained monomorphic ventricular tachycardia. DC shock of 300 joules was performed. After recovery to sinus rhythm, premature ventricular beats were frequently observed and lidocaine was administered intravenously. However, as this treatment was ineffective for ventricular arrhythmias, cibenzoline of 200 mg/day was administered in addition to diuretics and nitrates. In Holter ECG recorded on March 18, 3,516 ventricular premature beats, 53 couplets and two triplets were observed. Thus, cibenzoline was partially effective and the dose was increased to 300 mg/day. Moreover, 5 mg metoprolol was added and was increased gradually to 20 mg/day. A diagnosis of cardiac sarcoidosis was made and 40 mg prednisolone was started from April 7. After the combination therapy, Holter ECG on April 23 showed 1,716 premature ventricular beats and 31 couplets; that on August 28 showed only 163 premature ventricular beats a day. However, the cardiothoracic ratio in the chest X-ray and left ventricular dimension and ejection fraction determined by echocardiography remained unchanged, while angiotensin-converting enzyme decreased to within normal range (to 6 U/ml). Up to April 1993, the dose of corticosteroids is 10 mg/day, and 300 mg cibenzoline and 20 mg metoprolol has been continuously administered. This patient is still alive 21 months after starting combination therapy and being treated in the outpatient clinic, although she still feels slight exertional dyspnea.

Discussion

The major cause of death of sarcoidosis is cardiac involvement. Some ECG abnormalities are found in 22–51% of patients with sarcoidosis (3). Various arrhythmias are observed in patients with cardiac sarcoidosis and the most common cause of death has been heart block (4). However, Sekiguchi et al reported that pacemaker implantation reduces the death rate from heart block in cardiac sarcoidosis in Japan, and that heart failure and ventricular arrhythmias are increasing by the causes of death (6). The ventricular arrhythmias are sometimes difficult to control in cardiac sarcoidosis. Large doses of procainamide or diphenylhydantoin have been used (4). In the present patient, the ventricular tachyarrhythmias were sometimes polymorphic. The mechanism of ventricular tachycardias in the present patient was unknown; there was no mineral imbalance and no drug intake, but the QT interval was slightly long. The slightly long QT interval may be caused by diffuse myocardial involvement and the multiple myocardial lesion may cause polymorphic ventricular tachycardias. Since lidocaine (class Ib) infusion was ineffective for the treatment of ventricular arrhythmias in the present patient, cibenzoline was chosen as the drug of class la according to Vaughan-Williams’ classification (7). The ventricular arrhythmia in the present patient was reduced after

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<td>Cibenzoline</td>
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<td>Metoprolol</td>
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Table 1. Clinical Course of Arrhythmias

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<th>PVC</th>
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<td>couplet</td>
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<td>53/day</td>
<td>31/day</td>
<td>0/day</td>
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<tr>
<td>VT</td>
<td>678/day</td>
<td>2/day</td>
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ISDN: isosorbide dinitrate, PVC: premature ventricular beat, VT: ventricular tachycardia.
administration of cibenzoline and furthermore decreased after combination therapy with low-dose metoprolol and corticosteroids. In some patients with cardiac sarcoidosis, remission of the cardiac lesion and improvement of wall motion abnormalities have been observed after corticosteroid therapy (8). These patients usually have an active myocardial sarcoid lesion and the serum angiotensin-converting enzyme level is high. However, in the present patient, CRP and the erythrocyte sedimentation rate were normal, and serum-angiotensin converting enzyme was in the upper limit, although serum angiotensin-converting enzyme decreased to within normal range after start of corticosteroid therapy. Therefore, the suppression of ventricular arrhythmia may be mainly due to cibenzoline and/or low-dose beta blocker, while corticosteroids may partially contribute to the beneficial effect. It has been reported that in patients of polymorphic ventricular tachycardias with myocardial ischemia, class Ia drugs are often effective (9). Similarly, a class Ia drug, cibenzoline in the present case, was effective for the treatment of polymorphic ventricular tachycardia.

On the other hand, recently, low-dose beta blockers have been used for the treatment of heart failure; they are not only effective for symptom relief but also for improvement of the prognosis. The efficacy may depend on the upregulation of beta receptors and the cardiac protective action of beta blockers. These beneficial effects of beta blockers for the failed heart and combination therapy of low-dose beta blockers with cibenzoline and corticosteroids may contribute in the long term to a good prognosis for patients with severe myocardial involvement of sarcoidosis.

References
2) Longpore WT, Freiman DG. Study of sarcoïdosis on combined investigation of 160 cases including 30 autopsies from Johns Hopkins Hospital and Massachusetts General Hospital. Medicine 31: 1, 1952.
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